Remarks

With this response, Claims 35-101 are pending. By way of the present amendment, Claims 1-34 have been cancelled without prejudice or disclaimer of the underlying subject matter, and new Claims 35-101 have been added. No new matter enters by way of these amendments or additions. Support for these amendments can be found throughout the claims and specification as originally filed. For instance, see the original claims, paragraphs [0014], [0017], [0018], and [0019] of the specification, and the examples.

I. Rejection under 35 U.S.C. § 103(a)

Claims 1-22 and 32-33 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Navarro *et al.* ("Navarro") taken with Eng and WO 96/40196. This rejection is respectfully traversed, and to the extent that it applies to the new claims, reconsideration is requested for at least the reasons that follow.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on applicant's disclosure. *See* M.P.E.P. §§2143.01 and 2143.03.

The present invention is drawn to methods for reducing food intake, methods for reducing the appetite of a subject, and methods for lowering a plasma lipid. The methods of the presently claimed invention generally comprise peripherally administering to a subject an effective amount of an exendin.

Initially, Applicants respectfully disagree with the Examiner's characterization of the art. By way of example, the Examiner asserts that Navarro discloses the "intracerebroventricular (I.C.V.) administration of GLP-1 (7-36) amide in combination with exendin-3 and exendin-4 in a broad range of doses (0.2, 1, 5, 25, 100, and 500 ng) which resulted in marked decrease of both food and water intake." *Office Action mailed*

March 5, 2003, Paper No. 35, page 3. Further, the Examiner repeatedly refers to disclosures in the art of the use of "exendins and exendin antagonists including amylin agonist and CCK." *Id.* at page 4, 5.

In this regard, Applicants note that nowhere does Navarro disclose or suggest the use of exendin-3. Rather, Navarro discusses exendin-4 and exendin (9-39), which is a GLP-1 antagonist. Further, Applicants note that nowhere does Navarro disclose or suggest the combined use of GLP-1 (7-36) amide and exendin-4. Rather, Navarro discusses the I.C.V. administration of exendin-4 alone, *i.e.*, not in combination with GLP-1 (7-36) amide. Navarro does, however, discuss the I.C.V. administration of exendin (9-39), a GLP-1 antagonist, prior to the I.C.V. administration of GLP-1 (7-36) amide or the I.C.V. administration of exendin-4 for the experimental purpose of attempting to antagonize the effect of GLP-1 or exendin-4 with exendin (9-39). Further, the examiner's references to "exendin antagonists including amylin agonist and CCK" are confusing. The Examiner provides no teaching that would link amylin agonists or CCK to exendin antagonist activity, and, in fact, amylin agonists and CCK are not known by Applicant to have any exendin antagonist (or agonist) activity whatsoever. Moreover, the Examiner's reference to the relation of exendin antagonists to the present invention is unclear.

Nonetheless, whatever else Navarro does disclose, it does not disclose the peripheral administration of an exendin, much less the ability of exendins to reduce the food intake, appetite, or a plasma lipid of a subject following peripheral administration. Eng and WO 96/40196 do nothing to remedy the deficiencies of Navarro in this respect. Neither secondary reference teaches, discloses, or suggests the use or ability of exendins to reduce the food intake, appetite, or a plasma lipid level of a subject following peripheral administration.

In a proper obviousness determination, the changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention. *See In re Chu,* 36 U.S.P.Q.2d 1089, 1094 (Fed. Cir. 1995). This includes what could be characterized as simple changes. *See, e.g., In re*

Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984) (Although a prior art device could have been turned upside down, that did not make the modification obvious unless the prior art fairly suggested the desirability of turning the device upside down.).

Only when the prior art teaches or suggests the claimed invention does the burden fall on the applicant to rebut that *prima facie* case. *See In re Dillon,* 16 U.S.P.Q.2d 1897, 1901 (Fed. Cir. 1990) (in banc), *cert. denied,* 500 U.S. 904 (1991). However, a *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention.

As such, it is respectfully submitted that the Examiner's conclusion of obviousness is based on improper reasoning and a mischaracterization of the art. No suggestion to modify the cited references has been found in the cited references or pointed out to Applicant from the general knowledge of one of ordinary skill in the art. For at least these reasons, the Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. § 103. Even assuming *arguendo*, that a *prima facie* case of obviousness has been established, Navarro in fact teaches away from the present invention based on the finding that GLP-1 (7-36) amide does not "modify food and water intake" following peripheral administration.

More specifically, Navarro discusses the intraperitoneal administration of GLP-1 (7-36) amide, but does not disclose or suggest the intraperitoneal administration of exendin-4 or exendin (9-39). Further, with respect to the intraperitoneal administration of GLP-1 (7-36) amide, Navarro teaches that the acute or subchronic peripheral administration of GLP-1 (7-36) amide does not modify food and water intake, although a dose-dependent loss of body weight gain may be observed 24 hours after acute administration of higher doses (2 X 1,000 ng of GLP-1(7-36) amide / 100 g of body weight) of the peptide. *See Navarro,* Abstract and page 1985.

In sum, it is submitted that the prior art of record provides no suggestion or motivation to one of ordinary skill in the art to modify the teachings of Navarro to arrive at the present invention. The cited references do not disclose or suggest the peripheral administration of an exendin, much less the ability of exendins to reduce the food intake,

appetite, or a plasma lipid level of a subject following peripheral administration. As such, the cited references do not render the present claims obvious.

For at least the foregoing reasons, the Examiner's characterization of the art is traversed, and it is respectfully submitted that all of the pending claims are non-obvious over the prior art of record, since at a minimum they include or suggest the aforementioned limitations. As such, withdrawal of this rejection is respectfully requested.

II. Objection to the Claims

Claims 19 and 32-33 are objected to due to the recitation of the acronym CCK. Use of the full terminology at least in the first occurrence is requested. Although Applicants maintain that one of skill would clearly understand the scope of the claims, in order to facilitate prosecution, the newly presented claims recite "cholecystokinin." However, such amendment does not narrow the scope of the claim in any respect. As such, withdrawal of this objection is respectfully requested.

Conclusion

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objection and rejection of the claims, and to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-6111 should any additional information be necessary for allowance.

Respectfully submitted,

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Date: August 5, 2003

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